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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,760	09/12/2003	Andrea Liebmann-Vinson	020187.0238	5991

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EXAMINER	
FEELY, MICHAEL J	

ART UNIT	PAPER NUMBER
1712	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,760	LIEBMANN-VINSON ET AL.	
	Examiner	Art Unit	
	Michael J. Feely	1712	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29 and 32-37* is/are rejected.

7)☒ Claim(s) *30 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0204*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 1-7, 15-24, and 32-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Genzer et al. (US Pat. No. 6,423,372).

Regarding claims 1-7, 15, and 16, Genzer et al. disclose: *(1)* a method for producing a surface with enhanced cell-adhesive properties, comprising

(a) applying a stress to a flexible polymeric matrix (column 2, lines 37-48);

(b) maintaining said flexible polymer matrix as a strained matrix (column 2, lines 37-48);

(c) modifying the surface of said strained matrix by grafting a self-assembled mono-layer onto said strained matrix, said self-assembled mono-layer comprising at least one functional group (column 2, lines 37-48); and

(d) coupling at least one cell-adhesive molecule to said at least one active intermediate group on said self-assembled mono-layer (column 4, lines 10-42);

(2) wherein said strained flexible polymer matrix is released after said self-assembled mono-layer becomes grafted on the surface and prior to the addition of said at least one cell-adhesive molecule (column 2, lines 37-48; column 4, lines 10-42);

(3) wherein said strained flexible polymer matrix is maintained as a strained matrix until at least one cell-adhesive molecule has been coupled to said at least one active intermediate group of said self assembled mono-layer (column 2, lines 37-48; column 4, lines 10-42);

(4) wherein said self-assembled mono-layer comprises an alkylsilane derivative represented by $RSiX_3$, R_2SiX_2, or R_3SiX_3, wherein X is chloride or alkoxy, and R is a carbon chain having said at least one functional group (column 3, line 16 through column 4, line 9);

(5) wherein said at least one functional group of said self-assembled mono-layer are selected from amines, thiols, pyridyl, carboxyl, vinyl, sulfydryl, and aldehyde groups (column 3, line 16 through column 4, line 9);

(6) wherein said self-assembled mono-layer has native exposed functional groups (column 4, lines 10-30);

(7) wherein said self-assembled mono-layer has been chemically modified to have exposed functional group (column 4, lines 10-30);

(15) further comprising adjusting the density of said self-assembled mono-layer to control the density of said at least one cell adhesive molecule (column 4, lines 10-40); and

(16) further comprising the density of said at least one functional group on said self-assembled mono-layer to control the density of subsequently bonded at least one cell-adhesive molecule (column 4, lines 10-40).

Regarding claims 17-24, and 32-37, Genzer et al. disclose: *(17)* a device comprising a surface, said surface comprising:

(a) a flexible polymer matrix (column 2, lines 37-48);

(b) a mechanically self-assembled mono-layer (column 2, lines 37-48); and

(c) at least one cell-adhesive molecule coupled to said mechanically self-assembled mono-layer through at least one functional group on said self-assembled mono-layer (column 2, lines 37-48; column 4, lines 10-42);

(18) wherein said polymer matrix comprises polyorganosiloxane (column 2, lines 49-64); *(19)* wherein said polyorganosiloxane is polydimethyl siloxane (PMDS) (column 2, lines 49-64);

(20) wherein said self-assembled mono-layer comprises an alkylsilane derivative represented by $RSiX_3$, R_2SiX_2, or R_3SiX_3, wherein X is chloride or alkoxy, and R is a carbon chain having said at least one functional group (column 3, line 16 through column 4, line 9);

(21) wherein said at least one functional group of said self-assembled mono-layer are selected from amines, thiols, pyridyl, carboxyl, vinyl, sulfydryl, and aldehyde groups (column 3, line 16 through column 4, line 9); *(22)* wherein said self-assembled mono-layer is a chlorosilane-based oligomer or polymer (column 3, line 16 through column 4, line 9); *(23)* wherein said self-

assembled mono-layer is a trichlorosilane-based oligomer or polymer (column 3, line 16 through column 4, line 9);

(24) wherein said cell-adhesive molecule comprises one or more peptides or polypeptides (column 4, lines 31-42);

(32) wherein said polymer matrix is in the form of a three-dimensional scaffold having internal surfaces to which the self-assembled mono-layer is grafted and the cell-adhesive molecule is bonded (column 2, lines 49-64);

(33) wherein said polymer matrix is characterized by a strain of up to about 200% in response to an effective stress (column 5, lines 6-19);

(34) wherein said polymer matrix is characterized by a strain of up to about 100% in response to an effective stress (column 5, liens 6-19); *(35)* wherein said polymer matrix is characterized by a strain between about 40% and about 80% in response to an effective stress (column 5, lines 6-19); *(36)* wherein said polymer matrix is characterized in that it undergoes an elastic stress-strain response in which the polymer matrix returns to approximately its original length after application and cessation of the stress (column 5, lines 6-19); and

(37) which is susceptible to deformation upon application of mechanic forces such that adherent cells cultured in said device re subjected to the mechanical forces applied to an through the polymer matrix (column 6, lines 47-57).

3. Claims 1-7, 15-24, and 32-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Genzer et al. (US Pat. No. 6,770,323).

The applied reference has a common inventor with the instant application; however, the assignee and inventive entity is different. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Regarding claims 1-7, 15, and 16, Genzer et al. disclose: *(1)* a method for producing a surface with enhanced cell-adhesive properties, comprising

(a) applying a stress to a flexible polymeric matrix (column 5, line 6 through column 6, line 57);

(b) maintaining said flexible polymer matrix as a strained matrix (column 5, line 6 through column 6, line 57);

(c) modifying the surface of said strained matrix by grafting a self-assembled mono-layer onto said strained matrix, said self-assembled mono-layer comprising at least one functional group (column 5, line 6 through column 6, line 57); and

(d) coupling at least one cell-adhesive molecule to said at least one active intermediate group on said self-assembled mono-layer (column 7, line 50 through column 8, line 14);

(2) wherein said strained flexible polymer matrix is released after said self-assembled mono-layer becomes grafted on the surface and prior to the addition of said at least one cell-adhesive molecule (column 5, line 6 through column 6, line 57; column 7, line 50 through column 8, line 14);

(3) wherein said strained flexible polymer matrix is maintained as a strained matrix until at least one cell-adhesive molecule has been coupled to said at least one active intermediate group of said self assembled mono-layer (column 5, line 6 through column 6, line 57; column 7, line 50 through column 8, line 14);

(4) wherein said self-assembled mono-layer comprises an alkylsilane derivative represented by $RSiX_3$, R_2SiX_2, or R_3SiX_3, wherein X is chloride or alkoxy, and R is a carbon chain having said at least one functional group (column 6, line 58 through column 7, line 49);

(5) wherein said at least one functional group of said self-assembled mono-layer are selected from amines, thiols, pyridyl, carboxyl, vinyl, sulfydryl, and aldehyde groups (column 6, line 58 through column 7, line 49);

(6) wherein said self-assembled mono-layer has native exposed functional groups (column 7, lines 50-59);

(7) wherein said self-assembled mono-layer has been chemically modified to have exposed functional group (column 7, lines 50-59);

(15) further comprising adjusting the density of said self-assembled mono-layer to control the density of said at least one cell adhesive molecule (column 7, line 50 through column 8, line 2); and

(16) further comprising the density of said at least one functional group on said self-assembled mono-layer to control the density of subsequently bonded at least one cell-adhesive molecule (column 7, line 50 through column 8, line 2).

Regarding claims 17-24, and 32-37, Genzer et al. disclose: ***(17)*** a device comprising a surface, said surface comprising:

(a) a flexible polymer matrix (column 5, line 6 through column 6, line 57);

(b) a mechanically self-assembled mono-layer (column 5, line 6 through column 6, line 57); and

(c) at least one cell-adhesive molecule coupled to said mechanically self-assembled mono-layer through at least one functional group on said self-assembled mono-layer (column 7, line 50 through column 8, line 14);

(18) wherein said polymer matrix comprises polyorganosiloxane (column 5, lines 6-24); ***(19)*** wherein said polyorganosiloxane is polydimethyl siloxane (PMDS) (column 5, lines 6-24);

(20) wherein said self-assembled mono-layer comprises an alkylsilane derivative represented by $RSiX_3$, R_2SiX_2, or R_3SiX_3, wherein X is chloride or alkoxy, and R is a carbon chain having said at least one functional group (column 6, line 58 through column 7, line 49);

(21) wherein said at least one functional group of said self-assembled mono-layer are selected from amines, thiols, pyridyl, carboxyl, vinyl, sulfydryl, and aldehyde groups (column 6, line 58 through column 7, line 49); ***(22)*** wherein said self-assembled mono-layer is a chlorosilane-based oligomer or polymer (column 6, line 58 through column 7, line 49); ***(23)*** wherein said self-assembled mono-layer is a trichlorosilane-based oligomer or polymer (column 6, line 58 through column 7, line 49);

(24) wherein said cell-adhesive molecule comprises one or more peptides or polypeptides (column 8, lines 3-14);

(32) wherein said polymer matrix is in the form of a three-dimensional scaffold having internal surfaces to which the self-assembled mono-layer is grafted and the cell-adhesive molecule is bonded (column 5, lines 6-24);

(33) wherein said polymer matrix is characterized by a strain of up to about 200% in response to an effective stress (column 5, lines 25-42);

(34) wherein said polymer matrix is characterized by a strain of up to about 100% in response to an effective stress (column 5, liens 25-42); *(35)* wherein said polymer matrix is characterized by a strain between about 40% and about 80% in response to an effective stress (column 5, lines 25-42); *(36)* wherein said polymer matrix is characterized in that it undergoes an elastic stress-strain response in which the polymer matrix returns to approximately its original length after application and cessation of the stress (column 5, lines 25-42); and

(37) which is susceptible to deformation upon application of mechanic forces such that adherent cells cultured in said device re subjected to the mechanical forces applied to an through the polymer matrix (column 15, lines 24-31).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 8 rejected under 35 U.S.C. 103(a) as being obvious over Genzer et al. (US Pat. No. 6,423,372 **or** US Pat. No. 6,770,323) in view of Klaemer et al. (US Pat. No. 6,692,914).

The applied reference has a common inventor with the instant application; however, the assignee and inventive entity are different. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Regarding claim 8, the Genzer et al. references disclose that their surface-modified elastic substrate can be useful as a polymer brush; however, they do not explicitly disclose ***(8)*** that a functional group of polymer brush (of the self-assembled mono-layer) is activated.

Klaerner et al. also disclose a polymer brush, wherein the brush may contain a wide variety of probes. They disclose, "Typical polymer brush functionalities that are useful to covalently attach probes are chose among...O-acylisoureu intermediates from COOH-carbodiimide adducts," (column 29, lines 26-33). The teachings of Klaerner et al. demonstrate carbodiimide activated carboxyl groups are recognized in the art as suitable polymer brush

functionalities used for attaching probes thereto. In light of this, it has been found that the selection of a known material based on its suitability for its intended use supports a *prima facie* obviousness determination – *see MPEP 2144.07.*

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to activate the carboxyl functional groups of the polymer brush for the attachment of probes thereto, as taught by Klaerner et al., in the polymer brush of the Genzer et al. references because Klaerner et al. disclose that polymer brushes contain a wide variety of probes that are covalently attached to brush functionalities, including COOH functionalities which have been activated with carbodiimides to form O-acylisourea intermediates.

6. Claims 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Genzer et al. (US Pat. No. 6,423,372 **or** US Pat. No. 6,770,323) in view of Klaerner et al. (US Pat. No. 6,692,914) and Hendriks et al. (Pub. No.: US 2003/0035786).

Regarding claim 9-12, the combined teachings of Genzer et al. and Klaerner et al. disclose an activation step of carboxyl groups with carbodiimide; however, they do not explicitly disclose: ***(9)*** wherein the activation is done in the presence of a stabilizing compound; ***(10)*** wherein said carbodiimide is EDC; ***(11)*** wherein said stabilizing compound is selected from the group consisting of NHS, hydroxysulfosuccinate, and hydroxybenzotriazolohydrate; and ***(12)*** wherein said stabilizing compound is sulfo-NHS.

Hendriks et al. disclose biological adhesives wherein carboxyl groups are activated to provoke adhesion with tissue amino groups (paragraphs 0071-0076). The carboxyl group is activated with carbodiimides, such as EDC (paragraph 0076) to produce O-acylisourea groups.

In the presence of NHS or other stabilization agents, including sulfo-NHS (paragraph 0062), the O-acylisourea groups can be converted to carboxyl groups activated with the stabilizing agent (paragraph 0076). In light of this, it has been found that the selection of known materials based on their suitability for intended use supports a *prima facie* obviousness determination – *see MPEP 2144.07.*

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention perform activation according to the method of claims 9-12, as taught by Hendriks et al., in the combined teachings of Genzer et al. and Klaerner et al. because Hendriks et al. disclose that carboxyl groups are activated with carbodiimides *(such as EDC)* to produce O-acylisourea groups, and in the presence of NHS or other stabilization agents *(including sulfo-NHS)*, the O-acylisourea groups can be converted to carboxyl groups activated with the stabilizing agent, resulting in a biological tissue adhesive.

Regarding claims 13 and 14, Hendriks et al. do not provide specific concentrations of EDC and sulfo-NHS; however, Applicants fail to provide criticality for these ranges. One skilled in the art would have recognized that these concentrations are result-effective variables because a minimum amount of EDC would have been required to activate the carboxyl groups, an in turn, a minimum amount of sulfo-NHS would have been required to convert the EDC groups, in order to form the biological tissue adhesive. In light of this, it has been found that, "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation," – *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); and "A particular parameter must first be recognized as a result-

effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation," – *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to provide the claimed concentrations of EDC and sulfo-NHS in the combined teachings of Genzer et al., Klaerner et al., and Hendriks et al. because it has been found that it is not inventive to discover the optimum or workable ranges of known result-effective variable by routine experimentation.

7. Claims 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Genzer et al. (US Pat. No. 6,423,372 or US Pat. No. 6,770,323) in view of Chen et al. (Pub. No.: US 2002/0182633).

Regarding claims 25-29, the Genzer et al. references disclose the use of peptides as cell-adhesive molecule in molecular brushes; however, they do not explicitly disclose the use of: ***(25)*** a polypeptide as an extracellular matrix (ECM) molecule; ***(26)*** wherein said ECM is laminin; ***(27)*** wherein said ECM is fibronectin; ***(28)*** a polypeptide as an antibody or antigen-fragments thereof; and ***(29)*** a polypeptide as a growth factor.

The teachings of Chen et al. *(see paragraph 0042)* demonstrate that all of these specific polypeptide species are recognized in the art as *well known* binding agents used to undergo biological binding with a particular biological molecule. In light of this, it has been found that the selection of a known material based on its suitability for its intended use supports a *prima facie* obviousness determination – *see MPEP 2144.07.*

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use any of the polypeptide species set forth in claims 25-29 as the binding agent in the Genzer et al. references because the teachings of Chen et al. demonstrate that all of these species are recognized in the art as *well known* binding agents used to undergo biological binding with a particular biological molecule.

Allowable Subject Matter

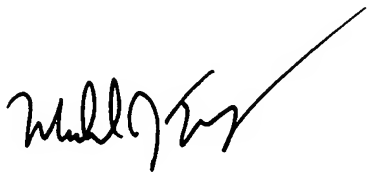
8. Claims 30 and 31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael J. Feely whose telephone number is 571-272-1086. The examiner can normally be reached on M-F 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Randy Gulakowski can be reached on 571-272-1302. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael J. Feely
Primary Examiner
Art Unit 1712

September 6, 2005